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Value of Certain Tests for Diagnosis and Prognosis in Chronic Nephritis

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THE VALUE OF CERTAIN TESTS FOR DIAGNOSIS AND PROGNOSIS IN CHRONIC NEPHRITIS.

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Numerous tests have been devised from time to time in order o make an early diagnosis or prognosis in chronic nephritis. Also y a study of the responses to certain tests attempts have been nade in recent years to classify the different types of chronic ephritis.

Of these different tests the examination of the urine for albumin nd casts and the determination of the blood-pressure have been sed pretty generally, especially for making a diagnosis of renal rouble. Recently, Rowntree and Geraghty[1] devised the now wellnown test which depends upon the elimination of phenolsulphonehthalein in the urine. Since its origin a considerable amount of work has been done on this test in regard to its ability to demonstrate chronic nephritis in the early stages or to make an accurate prognosis of the eventual outcome.

More recently Folin and Denis[2] have devised a technique for determining the non-protein nitrogen content of the blood which has given a fresh stimulus to this well-known method for studying renal disease and made it practical for clinical use. As a result, reports are coming from several clinics on the value of the nonprotein nitrogen content of the blood in diagnosis, prognosis, and classification of chronic nephritis.

For years the study of the kidneys' ability to excrete sodium chloride and various forms of nitrogen has been carried on. Usually these studies have been made by a quantitative determination of the intake in the food and the output in the urine of sodium chloride and nitrogen. It has been found that the ability of the individual to put out in the urine salt and nitrogen varies in different types and stages of nephritis. Widal,[3] Müller,[4] Monakow,[5] and others have attempted to arrange the cases into groups according to the retention of one or the other of these substances.

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[1] Jour. Pharm. and Exp. Ther., 1910, i, 579.

[2] Jour. Biol. Chem., 1912, xi, 527.

In one group these authors place the cases with salt retention and normal nitrogen elimination. In another, the cases with nitrogen retention but fairly good salt elimination. Both of these groups present clinical symptoms according to these authors which are characteristic. Many of the cases, however, are a combination of the two types.

In order to test more rapidly the ability of the individual to excrete salt in the urine, Schlayer[6] suggested the addition of 10 grams of sodium chloride to the diet at one dose after the patient had reached a salt equilibrium by being on a known diet for several days. In a normal individual this added salt should appear in the urine in twenty-four hours according to some authors, or at most in forty-eight hours. Monakow[7] devised a similar test to show the ability to put out nitrogen, which consisted in giving 20 grams of urea at one dose under similar circumstances. The nitrogen content of this urea, approximately 10 grams, should also be excreted in twenty-four to forty-eight hours by a normal individual.

Of course, it is possible that an individual might excrete the full amount of salt and nitrogen contained in the daily diet and yet fail to put out properly the excess of these substances given at one time. Doll and Siebeck[8] have emphasized this point in some recent work. However, experience has shown that these two tests offer a fairly good guide to the ability of the kidneys to take care of salt and nitrogen, and they have been used in recent years quite extensively for this purpose.

Recently, Ambard and Weil[9] have offered a method for determining salt and urea retention which consists in finding the blood content of these substances at a given time and their output in the urine at the corresponding time. It is hoped in this way the salt and nitrogen retention may be more readily determined.

Many other tests have been suggested for renal study, but those mentioned above seem to have received most attention in recent literature. Foremost among the workers on nephritis is Schlayer, who, with his assistants, has tried out many tests experimentally and clinically, including the lactose test of Voit[10] and the potassium iodide test of Duckworth.[11] More recently Hedinger and Schlayer[12] have been studying the work of the kidney by means of test meals, which are given for several days. The response of the kidneys at different periods of the day is carefully studied, and seems to be of both diagnostic and prognostic importance.

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[3] La Semaine Médicale, 1905, xxv, 313.

[4] Verhandl. der Deutsch. path. Gesellschaft, Moran, 1905.

[5] Deutsch. Archiv. f. klin. Med., 1914, cxvi, 1.

[6] Ibid., 1910–11, cl, 333.

[7] Ibid., 1911, cii, 248.

[8] Ibid., 1914, cxvi, 549.

[9] Jour. de phys. et de path. gen., 1912, xiv, 753.

[10] Deutsch. Arch. f. klin. Med., 1897, lviii, 545.

[11] Bartholomew's Hosp. Rep., 1867, iii, 216.

[12] Deutsch. Arch. f. klin. Med., 1914, cxiv, 120.

Since the opening of the Peter Bent Brigham Hospital the cases suspected of having chronic nephritis have been studied by a variety of tests. Up to the present time most attention has been paid to the blood-pressure, urinary examinations, phenolsulphonephthalein excretion, non-protein nitrogen content of the blood, and the ability to excrete in the urine added amounts of salt and urea given by the mouth. At the present time studies are being made on the cases of chronic nephritis by means of Schlayer's test diets, with modifications, and the Ambard and Weil method for determining salt and urea retention.

A sufficient number of cases of chronic nephritis have been studied by all of the six tests mentioned above to make a comparison of them of interest in order to decide on the value of these different tests for diagnosis, prognosis, and the purpose of classification. In all, over 100 cases diagnosed eventually as chronic nephritis have been studied by most of these tests. In only 40, however, have the tests been completed in all their details, and therefore this report will be limited to these 40 cases. It may be said, however, that the other cases in which some one or part of a test was lacking, apparently responded to the tests similarly to the forty reported.

The data collected in the accompanying table was obtained from the medical records of the hospital, and represent results obtained by a number of men on the staff either in their routine work or in some special study. The entrance blood-pressure is recorded, as it became evident that the pressure in most cases in which it was elevated fell after rest in the hospital. This reading also is probably nearer to that which would be found on meeting the patient in practice.

In the report on the urine the general impression from several examinations was recorded; for it is so well known that a single examination of the urine may not show albumin and casts which will be present on subsequent examinations.

The amount of non-protein nitrogen in the blood was determined by the method of Folin and Denis and the amount found on the first examination recorded; for in many of the cases attempts were made to change the amount by variations in the diet.

The phenolsulphonephthalein test has been done by the method originally suggested by Rowntree and Geraghty and the total excretion for two hours recorded. The first estimation after entrance was taken, and therefore it must be borne in mind that if passive congestion of a severe grade were present the output may have been considerably lower for that reason.

Hospital No.	Systolic pressure.	Urine.		Blood nitrogen per 100 c.c.	Per cent. 'phthalein in 2 hours.	Grams of NaCl above control.		Grams of nitrogen above control.		Complications.
		Albumin.	Casts.			1st day.	2d day.	1st day.	2d day.	
1443	225	+	Rare	27.2 mgs.	33	5.3	−0.3	9.6	0.0	Cardiac; no edema.
1358	145	+	+	46.0 mgs.	6	4.8	0.9	1.0	−1.2	None; no edema.
1340	225	+	+	35.2 mgs.	38	1.2	3.2	3.0	−0.8	None; no edema.
1023	258	+	+	36.0 mgs.	30	1.0	1.0	3.0	1.0	None; edema.
1197	225	+	+	39.0 mgs.	54	0.0	2.0	2.0	2.0	None; no edema.
1139	210	+	Rare	38.2 mgs.	51	3.5	3.0	4.0	1.5	None; no edema.
1170	230	+	+	34.2 mgs.	50	6.0	2.0	4.0	2.0	Cerebral; no edema; arteriosclerosis.
1154	258	+	+	30.9 mgs.	45	−2.9	−1.8	12.0	2.2	None; edema.
1178	128	+	+	20.0 mgs.	54	1.5	2.0	2.0	−0.5	Cirrhosis of liver; edema; arteriosclerosis.
1072	200	+	+	31.0 mgs.	51	2.0	1.0	4.0	4.0	Arteriosclerosis; no edema.
1365	185	+	+	36.5 mgs.	33	2.0	−0.1	7.2	3.7	Cardiac; edema.
1490	270	+	+	26.8 mgs.	34	−0.3	−3.8	5.4	2.3	Cardiac; no edema.
974	190	+	+	54.1 mgs.	25	1.0	0.0	8.0	8.0	None; no edema.
986	180	Rare	Rare	25.9 mgs.	36	2.6	−0.9	5.0	4.0	Cardiac; edema.
918	245	+	+	70.9 mgs.	14	0.5	−1.5	0.5	−6.0	None; edema.
1056	218	+	+	78.9 mgs.	0	1.0	−1.0	−2.0	3.0	Arteriosclerosis; no edema.
1075	192	+	+	23.8 mgs.	55	−1.0	3.0	8.0	1.15	None; edema.
1885	154	+	+	39.0 mgs.	24	.0	2.1	2.0	2.0	Cardiac; edema.
1918	254	+	+	31.0 mgs.	49	.0	2.5	3.0	2.0	None; no edema.
1948	220	+	0	25.0 mgs.	65	4.5	5.5	9.0	−1.5	Cardiac; no edema.
2077	255	+	+	23.0 mgs.	52	2.0	−2.0	8.0	2.0	Myocarditis; no edema.
2074	164	+	+	40.0 mgs.	18	1.5	1.5	1.0	1.0	None; no edema.
1898	200	+	+	32.0 mgs.	43	2.5	1.0	6.0	9.0	Cardiac; edema.
1696	170	+	+	16.5 mgs.	54	0.0	3.0	4.0	−2.0	Cardiac; no edema.
1814	186	+	0	33.0 mgs.	42	0.0	−3.5	5.0	4.0	Cardiac; edema.
1661	190	+	+	38.0 mgs.	42	2.0	1.8	9.0	4.0	Diabetes; no edema; myocarditis.
1459	220	+	+	21.3 mgs.	48	0.0	3.0	3.0	1.0	None; edema.
1738	190	+	Rare	25.0 mgs.	50	3.0	1.5	8.0	2.0	None; no edema.
1804	260	+	Rare	33.0 mgs.	59	0.0	2.5	6.5	−1.0	Myocarditis; no edema.
1754	122	+	+	36.0 mgs.	28	−0.5	0.5	0.5	−0.5	None; edema.
1624	150	+	+	40.0 mgs.	28	1.0	2.0	6.0	2.0	None; edema.
1608	230	+	0	76.2 mgs.	15	−4.0	−2.0	2.0	0.0	Lead arteriosclerosis; no edema.
1821	188	+	+	33.0 mgs.	18	4.5	1.0	0.0	0.0	None; no edema.
1760	250	+	+	28.0 mgs.	30	−0.5	0.0	1.0	−1.0	None; no edema.
624	220	Rare	Rare	25.4 mgs.	45	−2.5	−4.7	3.9	3.0	Arteriosclerosis; edema.
684	210	+	Rare	25.0 mgs.	65	3.2	4.2	7.0	4.0	None; no edema.
762	180	+	+	50.0 mgs.	35	1.0	−0.5	4.0	1.0	None; edema.
782	185	Rare	0	33.2 mgs.	58	2.0	5.0	9.0	1.8	Acute rheumatism; no edema.
817	212	Rare	Rare	31.8 mgs.	56	1.8	1.6	5.0	2.0	None; no edema.
548	190	+	Rare	23.2 mgs.	45	3.3	−0.1	10.0	3.0	Cardiac; no edema.

For several days before giving the extra amounts of sodium hloride and urea the patients were placed on a known diet and heir ability to put out salt and nitrogen recorded until the amount ecame practically constant. The amount of salt or nitrogen in xcess of that excreted on the day preceding the dosage was recorded or the first and second twenty-four-hour periods following the dose. n some instances the amount excreted on one or the other day vas less than that on the control day. In such instances a minus ign is placed before the figure.

In order to group the cases according to their response to these ests the excretion was considered normal if 8.5 grams of the 10 grams of added salt or nitrogen were put out in the forty-eight hours. It was considered a slight retention if between 4.5 grams and 8.5 grams were excreted. If less than 4.5 grams were put out n the forty-eight hours the retention was considered marked.

Clinically the cases in the accompanying table varied from the edematous patients with normal or slightly elevated blood-pressures and considerable evidence of active renal disturbance without uremic symptoms, to the cases with high pressure, shortness of breath, marked uremic phenomena, pronounced eye-ground changes, and with or without edema.

The severest cases of nephritis are not included in this list because it was not considered advisable to give them added salt and urea, and because frequently it was impossible to feed them with enough regularity to find their normal elimination. It is interesting to note that cases with the same clinical course frequently showed at autopsy a form of chronic nephritis quite different from each other.

Of these 40 cases representing different types and grades of chronic nephritis, 37 showed a systolic blood-pressure of 150 or above, which is usually considered as abnormal. In 3 cases the pressure was apparently normal. It seems fair, therefore, to decide that an elevated blood-pressure occurs with sufficient frequency to be a good aid in diagnosis. In another work, Smillie and Frothingham[13] have shown that the height of the blood-pressure is not a definite guide to the severity of the nephritis. Although it tends to be slightly higher on an average in the severer cases, the individual variation is so marked that very little aid for prognosis can be obtained from it.

The 3 cases with normal blood-pressure did not fall into any one clinical group, and cases with quite different clinical signs showed an elevated blood-pressure. Therefore, it is evident that the blood-pressure determination is not of much value in regard to the clinical classification of chronic nephritis.

In 36 of the cases albumin was present in varying amounts in all or most of the examinations; in 4 it was present so infrequently that its presence might have been overlooked even after several tests; 27 cases showed casts most of the time, 9 only rarely, and 4 not at all. It is evident that albumin is almost as common a sign in chronic nephritis as a high blood-pressure, but that casts do not occur so frequently. On account of the presence of albumin and casts in other conditions than chronic nephritis the occurrence of them in the urine is not of sure diagnostic value, but it offers a good guide for further study, and few cases would be missed by these tests alone if more than one examination were made.

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[13] Arch. Int. Med., 1915, xv, 204.

It is well known that some of the most severe cases bordering on uremia show little or no albumin or casts in the urine, so that for prognosis these tests are of practically no value.

The number and character of the casts, however, are of considerable value as a guide to the amount of renal destruction actually going on at a given time. On the other hand, a large amount of albumin may mean a considerable amount of active renal destruction, or it may simply show a leakage through the kidney of serum albumin. Cases of a similar clinical type, namely, those in younger people with considerable edema, usually show considerable albumin and many casts in the urine, but other clinical types of nephritis also at times show much albumin and many casts. Therefore, for the purpose of a clinical classification of chronic nephritis, the presence or amount of albumin and casts in the urine is not of much assistance.

Thirty mgm. or less per 100 c.c. of blood was considered the normal content of non-protein nitrogen for the blood. With this as a standard, 26 of the 40 cases showed an increase over the normal of non-protein nitrogen. In 14 cases the amount fell within the normal limits. It is evident, therefore, that cases which are recognized as chronic nephritis may have a normal non-protein nitrogen content in the blood. Thus, for an early diagnosis of chronic nephritis this test is not of great value. On the other hand, in patients whose unconsciousness is due to uremia the non-protein nitrogen is always elevated in our experience, and, therefore, in this type of case the test is of considerable value in making a differential diagnosis. For prognosis this test is of considerable value. There seems to be a fairly direct relation between the severity of the nephritis and the amount of non-protein nitrogen in the blood as was shown in a study of these and other nephritis cases by Frothingham and Smillie.[14]

The cases in this series with the same clinical type of chronic nephritis varied from a normal amount to a marked elevation of the non-protein nitrogen content of the blood, also some of the cases of all the clinical types included showed an elevated and others a normal blood nitrogen. It was felt, therefore, that this test would be of little value in the classification of chronic nephritis.

Fifty per cent. or more of the phenolsulphonephthalein should e excreted under normal conditions in two hours. Of these 40 ases 26 showed a diminished 'phthalein excretion and 14 put out normal amount. This series showed, therefore, what has been ound repeatedly, that certain cases of chronic nephritis have, specially in the early stages, a normal 'phthalein excretion. There-ore, for diagnosis in the early stages of the disease this test is not eliable. Furthermore, the diminished 'phthalein excretion in some f the cases may have been due to passive congestion.

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[14] Loc. cit.

For prognosis the test is more valuable provided that passive ongestion is ruled out. This is specially true in the cases in which he 'phthalein elimination is markedly diminished. In this class f cases other tests and the clinical findings usually point to a severe ephritis. Occasionally for some unexplained reason in the severe ases of chronic nephritis the 'phthalein output may be practically ormal. In some at least of all the clinical types of chronic nephritis tudied the 'phthalein elimination was lowered, and so for the purpose of classification of chronic nephritis this test is not of value.

Of the 40 cases only 1 showed a normal excretion of the extra odium chlorine; 8 had what has been arbitrarily called a moderate etention of the added salt, and 31 were very markedly unable to xcrete it. Apparently, therefore, disturbance in the ability to liminate salt is a common occurrence in all types of chronic nephritis nd may be considered a good diagnostic sign. For prognosis this est is not of much value, because the kidneys apparently lose the bility to excrete the added salt in appreciable amounts before the ther tests suggest that the nephritis has become severe. Although ther authors have attempted to group the cases of chronic nephritis omewhat in their relation to sodium chloride excretion, it was not ossible to do so in this series, because practically all the cases, ncluding a variety of clinical types, showed the inability to xcrete it.

Fifteen of the 40 cases excreted the added urea well, 9 fairly well, ccording to the set standard, and 16 showed a marked inability o excrete it. This test, therefore, can not be depended upon for aking an early diagnosis. For prognosis the test is more useful, s in all but 3 of the 16 cases, which showed a marked retention, he other evidence pointed to a severe grade of nephritis.

This test has not been of value for classifying chronic nephritis, or in cases which are apparently of the same type the excretion f the urea varies considerably. In all but 3 of the 16 cases with arked urea retention the salt retention was also marked. In these cases the salt retention was moderate. Therefore, although there ere some cases with what might be termed pure salt retention, here were none in which there could be said to be a pure nitrogen etention.

Twenty-five of the 40 cases showed edema at entrance. Of course, cannot be definitely determined in how many of these cases the edema was due to cardiac disturbance. A list of the important complications to the chronic nephritis is also added in the table.

From this study it seems fair to conclude that the blood-pressure determination, repeated urinary examinations, and a study of the ability of the kidney to excrete extra sodium chloride are the most reliable tests for making an early diagnosis of chronic nephritis.

For prognosis in chronic nephritis the determination of the non-protein nitrogen in the blood, the excretion of phenolsulphonephthalein in the urine, and the ability to excrete extra nitrogen in the urine are the most useful tests.

By means of these tests it is not possible to group the cases of chronic nephritis in relation to their clinical appearance. Further study on the relation of these tests to the pathological lesions in the kidney is being carried on.

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